UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,668	02/02/2004	Susan C. Wright	ABSALUS-08602	2158

7590 07/12/2006

MEDLEN & CARROLL, LLP
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,668	WRIGHT ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *20-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Election filed on April 25, 2006 in response to the Restriction Requirement of November 30, 2005 has been entered. Applicant's election of Group I, claims 1-19, as specifically drawn to a composition comprising an isolated amino acid sequence that comprises a portion of SEQ ID NO: 4, wherein said portion comprises SEQ ID NO: 6 or SEQ ID NO: 7 has been acknowledged.

Applicant's election of Group I, with traverse, is acknowledged. The traversal is on the grounds that it is improper to restrict the inventions of Groups IV-V because the Office simply has no statutory authority whatsoever to reject a claim for misjoinder of invention (the per se definition of restriction as applied to a single claim, as the Examiner has here done, e.g., for claims 31-35). As such, Applicants request rejoinder of Groups IV and V.

These arguments have been carefully considered and have been found persuasive. The inventions of Group IV and Group V are rejoined. However, in light of Applicants' election of Group I above, the rejoinder of Groups IV and V is essentially moot in the subject case.

The restriction requirement is therefore deemed to be proper and is made FINAL.

Claims 1-47 are currently pending.

Claims 20-47 have been withdrawn from consideration as being drawn to non-elected inventions.

Claims 1-19 are currently under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 1/03/2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandman et al. (US 6,274,138, 2001).

Bandman et al. teach a composition comprising an isolated mitochondrial amino acid sequence consisting of the instantly claimed amino acid sequence of SEQ ID NO: 4 (Columns 37-39 and below sequence comparison). In the instant case, the transitional phrase "comprises", which is synonymous with "including," "containing," or "characterized by," recited in the current claims is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.). Thus, Bandman et al. teaches a composition comprising a portion of SEQ ID NO: 4, wherein the portion comprises SEQ ID NO: 6 or SEQ ID NO: 7. Moreover, although Bandman et al. does not specifically teach that the polypeptide has activity chosen from DNA nuclease activity and cell killing activity, the claims are drawn to the product *per se* and inherently, such a polypeptide have activity chosen from DNA nuclease activity and cell killing activity. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

US6274138-B1.
Bandman O, Corley NC, Shah P;

```
  Query Match             100.0%;  Score 497;  DB 4;  Length 338;
  Best Local Similarity   100.0%;  Pred. No. 1.2e-51;
  Matches  100;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

1   KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 60
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
239 KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 298

61  IEKNLGIGKVSSFEEKMISDAIPELKASIKKGEDFVKTLK 100
    ||||||||||||||||||||||||||||||||||||||||
299 IEKNLGIGKVSSFEEKMISDAIPELKASIKKGEDFVKTLK 338


US6274138-B1.
Bandman O,  Corley NC,  Shah P;

  Query Match             100.0%;  Score 360;  DB 4;  Length 338;
  Best Local Similarity   100.0%;  Pred. No. 1.5e-39;
  Matches   72;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

1   KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 60
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
239 KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 298

61  IEKNLGIGKVSS 72
    ||||||||||||
299 IEKNLGIGKVSS 310
```

Claims 1-5, 8 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al. (WO 01/66689 A2, 2001).

Tang et al. teach a composition comprising an isolated amino acid sequence consisting of the instantly claimed amino acid sequence of SEQ ID NO: 4 (SEQ ID NO: 233 of WO publication, see below sequence comparison). With respect to the amino acid sequence, the WO publication teaches that the amino acids include, but are not limited to, both full length (comprising a signal sequence) and mature forms (without a signal sequence) (page 28, lines 19-20). Moreover, Tang et al. teach that the polypeptides may be operably linked to a targeting moiety such as an antibody which binds to a cell molecule (page 32, lines 1-14 and line 34 to page 33, line 25). For example, the WO publication teaches that the polypeptides may be operably linked to an antibody which specifically binds a target on pancreatic cells. In the instant case, the transitional phrase "comprises", which is synonymous with "including," "containing," or "characterized by," recited in the current

claims is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003) Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.). Thus, in view of the transitional phrase, Tang et al. teach a composition comprising a portion of SEQ ID NO: 4, wherein the portion comprises SEQ ID NO: 6 or SEQ ID NO: 7. Moreover, although Tang et al. does not specifically teach that the polypeptide has activity chosen from DNA nuclease activity and cell killing activity, the claims are drawn to the product *per se* and inherently, such a polypeptide have activity chosen from DNA nuclease activity and cell killing activity. Thus, the claimed peptide appears to be the same as the prior art. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

```
Novel human secretory protein, Seq ID No 233.
WO200166689-A2.
Tang YT,  Liu C,  Asundi V,  Xu C,  Wehrman T,  Ren F,  Ma Y,  Zhou P;
Zhao QA,  Yang Y,  Drmanac RT,  Zhang J,  Chen R,  Xue AJ,  Wang J;

1   KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 60
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
239 KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 298

61  IEKNLGIGKVSS 72
    ||||||||||||
299 IEKNLGIGKVSS 310

Novel human secretory protein, Seq ID No 233.
WO200166689-A2.
Tang YT,  Liu C,  Asundi V,  Xu C,  Wehrman T,  Ren F,  Ma Y,  Zhou P;
Zhao QA,  Yang Y,  Drmanac RT,  Zhang J,  Chen R,  Xue AJ,  Wang J;
1   KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 60
```

```
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
239 KAKAGAGSATLSMAYAGARFVFSLVDAMNGKEGVVECSFVKSQETECTYFSTPLLLGKKG 298

61  IEKNLGIGKVSSFEEKMISDAIPELKASIKKGEDFVKTLK 100
    ||||||||||||||||||||||||||||||||||||||||
299 IEKNLGIGKVSSFEEKMISDAIPELKASIKKGEDFVKTLK 338
```

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 9-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 01/66689, 2001) in view of Wang et al. (Cancer Research 1991; 51: 3353-3355).

Tang et al. teach, as applied to claims 1-5, 8 and 17 above, a composition comprising an isolated amino acid sequence comprising the instantly claimed amino acid sequence of SEQ ID NO: 6 and 7 (SEQ ID NO: 233 of WO publication, see below sequence comparison). With respect to the amino acid sequence, the WO publication teaches that the amino acids include, but are not limited to, both full length (comprising a signal sequence) and mature forms (without a signal sequence) (page 28, lines 19-20). Moreover, Tang et al. teach that the polypeptides may be operably linked to a targeting moiety such as an antibody, wherein the targeting moiety increases the biological activity of the polypeptide (page 32, lines 1-14 and line 34 to page 33, line 25). In addition, the WO document teaches that the

polypeptide is useful for the treatment of cancers including, but not limited to, liver cancer (page 53, lines 5-29).

Tang et al. do not explicitly teach that the antibody binds to liver cancer cells, wherein the antibody is Hepama-1.

Wang et al. teach a Hepama-1 antibody toxin conjugate. Specifically, the reference teaches that the hepatoma cytotoxicity of the conjugate was 500-fold higher as compared to the free toxin.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was to combine the polypeptide as taught by Tang et al. with an antibody such as Hepama-1 in view of the Wang et al.'s teachings that made to administer to a patient a mixture comprising a cyclic peptide and a liposome carrying a chemotherapeutic, such as adriamycin, in view of Penate-Medina *et al.*. One would have been motivated to do so because as taught by Penate-Medina *et al.*, CTT promotes liposome targeting to tumors in vivo (page 2, lines 7-8) and further, that CTT enhanced delivery of adriamycin-containing liposomes resulted in an improved killing of U937 leukemia and HT1080 sarcoma cells (page 1, lines 14-15). Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering to a patient a mixture comprising a cyclic peptide and a liposome carrying a chemotherapeutic, such as adriamycin, in view of Penate-Medina *et al.*, one would achieve a method for specific delivery and targeting of a chemotherapeutic for the treatment of cancer, wherein the chemotherapeutic as a result of the liposome and cyclic peptide show enhanced tumor uptake.

Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 01/66689, 2001) in view of Sherman et al. (2002/0022027, 2002).

Tang et al. teach, as applied to claims 1-5, 8 and 17 above, a composition comprising an isolated amino acid sequence comprising the instantly claimed amino acid sequence of SEQ ID NO: 6 and 7 (SEQ ID NO: 233 of WO publication, see below sequence comparison). With respect to the amino acid sequence, the WO publication teaches that the amino acids include, but are not limited to, both full length (comprising a signal sequence) and mature forms (without a signal sequence) (page 28, lines 19-20). Moreover, Tang et al. teach that the polypeptides may be operably linked to a targeting moiety such as an antibody,

wherein the targeting moiety increases the biological activity of the polypeptide (page 32, lines 1-14 and line 34 to page 33, line 25). In addition, the WO document teaches that the polypeptide is useful for the treatment of a variety of cancers including, but not limited to, liver cancer (page 53, lines 5-29).

Tang et al. do not explicitly teach that the polypeptide-antibody conjugate further comprises a cell internalization peptide and/or nuclear localization peptide.

Sherman et al. teach a composition comprising a Vpr polypeptide conjugated to a therapeutic molecule (ab). With regards to the Vpr peptide, the publication teaches that Vpr contains at least two nuclear localization signals and is capable of delivering molecules to the cell nucleus (page 1, 2nd column, paragraph 0006). With regards to the therapeutic molecule, Sherman et al. teach that the therapeutic molecules include, but are not limited to, polypeptides, polynucleotides and toxins (page 1, 1st column, paragraph 0007). Moreover, the publication teaches a method of killing a target cell and/or inhibiting cell proliferation or a target cell comprising administering a Vpr peptide conjugate or Vpr alone, wherein the Vpr conjugate is delivered into a cell and said cell is a cancer cell (abstract; page 1, 2nd column, paragraph 0008 and page 2, 1st column, paragraph 0010).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was to made to further attach a cell internalization/ nuclear localization peptide to the antibody-MDH conjugate as taught by Tang et al. in view of the Sherman et al.. One would have been motivated to do so because Sherman et al. teach that Vpr polypeptides conjugated to therapeutic molecules allows for the selective delivery of the therapeutic molecule within the cell, wherein the therapeutic molecule is released from the Vpr by protease cleavage of the Vpr conjugate. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by administering an antibody-MDH conjugate which further comprises a cell internalization/ nuclear localization peptide, one would achieve a method for specific delivery and targeting of MDH for the treatment of cancer.

Secondly, each of the agents, e.g., MDH-antibody conjugate and a Vpr polypeptide, have been individually taught in the prior art as being useful for the treatment of cancer. As such, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have

been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

Claims 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 01/66689, 2001) in view of Unger et al. (US 6,139,819, 2000).

Tang et al. teach, as applied to claims 1-5, 8 and 17 above, a composition comprising an isolated amino acid sequence comprising the instantly claimed amino acid sequence of SEQ ID NO: 6 and 7 (SEQ ID NO: 233 of WO publication, see below sequence comparison). With respect to the amino acid sequence, the WO publication teaches that the amino acids include, but are not limited to, both full length (comprising a signal sequence) and mature forms (without a signal sequence) (page 28, lines 19-20). Moreover, Tang et al. teach that the polypeptides may be operably linked to a targeting moiety such as an antibody, wherein the targeting moiety increases the biological activity of the polypeptide (page 32, lines 1-14 and line 34 to page 33, line 25). In addition, the WO document teaches that the polypeptide is useful for the treatment of a variety of cancers including, but not limited to, breast cancer (page 53, lines 5-29).

Tang et al. do not explicitly teach a conjugate comprising an amino acid sequence comprising SEQ ID NO: 6 or 7 operably linked to a first molecule that specifically bins to a cell molecule, wherein the first molecule is a ligand such as a vascular endothelial growth factor or fibroblast growth factor.

Unger et al. teach a composition comprising a contrast agent operably linked to a targeting ligand for the use in diagnostic applications, as well as therapeutic applications. With regards to the targeting ligand, the patent teaches that targeting agents include, but are not limited to, growth factors such as basic fibroblast growth factor and/or vascular endothelia growth factor (column 35, lines 24+). Specifically, the patent teaches that targeting ligands can be selected for targeting antigens, including antigens associated with breast cancer, such as fibroblast growth factor receptor (column 38, lines 13-31).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was to made to substitute an antibody as taught by Tang et al. for a growth factor ligand in view of Unger et al. for the purposes of targeting the peptide. One would have been motivated to do so because each of the targeting agents have been individually

taught in the prior art to be equivalents for targeting therapeutic compounds to antigens expressed on tumor cells. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by substituting an antibody as taught by Tang et al. for a growth factor ligand in view of Unger et al., one would achieve a peptide-growth factor ligand conjugate which can be used for the treatment of breast cancer.

Therefore, NO claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

BF
July 3, 2006

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER